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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	PAPER NUMBER
1652	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,692	NAYAR ET AL.	
	Examiner	Art Unit	
	SHERIDAN SWOPE	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *September 4 & October 14, 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0809;0909*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Request for Continued Examination of September 4, 2009 and Supplemental Response of October 14, 2009, in response to the action of March 4, 2009, are acknowledged. It is acknowledged that no claims have been cancelled, amended, or added. Claims 1-21 are pending and are herein reconsidered.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Double Patenting

Provisional rejection of Claims 1-21 under the judicially created doctrine of obviousness-type double patenting, as being unpatentable over Claims 1-3, 6, 8, 9, 12, 29, 31, and 32 of US 10/579,088 for the reasons explained in the prior action, is maintained.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons. For Claim 13, the phrase "initial activity" renders the claim indefinite. It is unclear whether said phrase means activity of the pre-lyophilized sample or activity of the initial lyophilized sample. The skilled artisan would not know the metes and bounds of the recited invention.

Regarding the phrase "recombinant human alpha-1-antityrpsin (rAAT)", the following comments are made. The functional limitations are defined by the specification [0021] as:

> "Criteria for stability (retained activity) and denaturation are demonstrated by assays known to those skilled in the art. Activity assays are based on the porcine pancreatic elastase inhibition assay reported by Beatty et al, 1980" (Examiner's emphasis).

Regarding the structural limitations, the specification states (pg 1, parg 1):

> "rAAT is a 395 amino acid protein of 44 kD, that is non-glycosylated and has an amino acid sequence identical to the human plasma protein (AAT) with the exception of an N-acetylmethionine residue at the amino terminus."

Applicants further assert, in the instant response, that the skilled artisan would know that human AAT is the protein set forth by GenBank protein Accession number AAB59375. Based on said disclosures of the prior art, the specification, and Applicants' response, it is concluded that "recombinant human alpha-1-antityrpsin (rAAT)" means the non-glycosylated form of the human plasma protein (AAT) sequence provided in Accession Nos. P01009 and AAB59375, with the exception of an N- acetylmethionine residue at the amino terminus, as set forth by:

> "MEDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVS IATAFAMLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNG LFLSEGLKLVDKFLEDVKKLYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKEL DRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKK LSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITG TYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLE AIPMSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQK".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Rejection of Claim 1-21 under 35 U.S.C. 112, first paragraph/enablement, for the reasons explained in the prior actions, is withdrawn for the following reasons. Based on the disclosures

of the prior art, the specification, and Applicants' response, it is concluded that "recombinant human alpha-1-antityrpsin (rAAT)" means the non-glycosylated form of the human plasma protein (AAT) sequence provided in Accession Nos. P01009 and AAB59375, with the exception of an N- acetylmethionine residue at the amino terminus, as set forth by:

"MEDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVS
IATAFAMLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNG
LFLSEGLKLVDKFLEDVKKLYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKEL
DRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKK
LSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITG
TYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLE
AIPMSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQK".

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 13 recites a composition "that retains at least 80% of initial rAAT activity upon storage under conditions that are, or are equivalent to, 50°C for 3 months". The specification fails to teach the skilled artisan how to make and use a composition having said limitations. Therefore, Claims 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 14 recites a composition "that retains at least 80% monomeric rAAT upon storage under conditions that are, or are equivalent to, 50°C for 3 months". The specification fails to teach the skilled artisan how to

make and use a composition having said limitations. Therefore, Claims 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

Written Description

Rejection of Claim 1-21 under 35 U.S.C. 112, first paragraph/written description, for the reasons explained in the prior actions, is withdrawn for the following reasons. Based on the disclosures of the prior art, the specification, and Applicants' response, it is concluded that "recombinant human alpha-1-antityrpsin (rAAT)" means the non-glycosylated form of the human plasma protein (AAT) sequence provided in Accession Nos. P01009 and AAB59375, with the exception of an N- acetylmethionine residue at the amino terminus, as set forth by:

"MEDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVS
IATAFAMLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNG
LFLSEGLKLVDKFLEDVKKLYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKEL
DRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKK
LSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITG
TYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLE
AIPMSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQK".

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This claim is directed to a genus of rAAT compositions "that retains at least 80% of initial rAAT activity upon storage under conditions that are, or are equivalent to, 50°C for 3 months". The specification teaches no such compositions. Moreover, the specification fails to describe any representative species of such compositions by any identifying characteristics or properties other than the functionality of being a rAAT composition "that retains at least 80% of initial rAAT activity upon storage under conditions that are, or are equivalent to, 50°C for 3 months". Given this lack of description of representative species

encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This claim is directed to a genus of rAAT compositions "that retains at least 80% monomeric rAAT upon storage under conditions that are, or are equivalent to, 50°C for 3 months". The specification teaches no such compositions. Moreover, the specification fails to describe any representative species of such compositions by any identifying characteristics or properties other than the functionality of being a rAAT composition "that retains at least 80% of monomeric rAAT upon storage under conditions that are, or are equivalent to, 50°C for 3 months". Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6-12, 17, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Hubbard et al, 1989 (IDS). Hubbard et al teach a preparation of the non-glycosylated mature form of human AAT having an N-terminal methionine (rAAT herein; pg 1350, parg 2). Hubbard et al further teaches lyophilization of lavage samples comprising said rAAT (pg 1350, parg 11). Therefore, Claims 1-4, 6-12, 17, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Hubbard et al, 1989.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-12, 17, 18, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Casolaro et al, 1987 in view of Eljamal et al, 1998. Casolaro et al teaches a >99.9% pure non-glycosylated mature form of human AAT having an N-terminal methionine (rAAT herein; pg 2016, parg 2-3). Casolaro et al does not teach a dry powder composition comprising their rAAT. As acknowledged by the specification [0004], Eljamal et al teaches a >99% pure dry powder formulation of AAT (Example 1; col 6, parg 6) and various drying techniques including buffers and surfactants (Section II, cols 3-7). It would have been obvious to a person of ordinary skill in the art to use the drying techniques of Eljamal et al to make a dry powder formulation of the rAAT of Casolaro et al. Motivation to do so is provide by the desire to store the dry powder formulation for further study of the rAAT of Casolaro et al. The expectation of success is high, as both the rAAT of Casolaro et al and the ATT drying techniques of Eljamal et al were well-

known in the art. Therefore, Claims 1-12 17, 18, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Casolaro et al, 1987 in view of Eljamal et al, 1998.

Claim 15, 16, 19, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Casolaro et al, 1987 and Eljamal et al, 1998 in view of Cochrane et al, 1983 and further in view of Krishnamurthy et al, 2002. The teachings of the combination of Casolaro et al and Eljamal et al are described above. Said combination does not teach a dry powder composition comprising rAAT and further comprising a reducing agent and/or an antioxidant, or a chelator. Cochrane et al teach that AAT is inactivated in the lungs of patients with ARDS and that this inactivation is due to oxidation (Fig 1 & 3). It would have been obvious to a person of ordinary skill in the art to include a reducing agent and/or an antioxidant, including a chelator, in the dry powder rAAT composition rendered obvious by Casolaro et al and Eljamal et al. Motivation to do so is provide by the desire to inhibit the oxidative inactivation of the rAAT when administered to patients with ARDS. The expectation of success is high, as the use of reducing agents, antioxidants, and/or a chelators to inhibit oxidative inactivation in therapeutic compositions was well-known in the art (Krishnamurthy et al; pg 367, parg 8). Therefore, Claims 15, 16, 19, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Casolaro et al, 1987 and Eljamal et al, 1998 in view of Cochrane et al, 1983 and further in view of Krishnamurthy et al, 2002.

Allowable Subject Matter

No claims are allowable.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
Primary Examiner, Art Unit 1652